REMARKS

Provisional rejection of Claims 37, 39-52 and 54-66 under obviousness-type double patenting

Claims 37, 39-52 and 54-66 are provisionally rejected under obviousness-type double patenting as being unpatentable over Claims 31-33 of copending U.S. application no. 09/079,569 (hereafter the "'569 application") which has published as U.S. Patent application 2003/0104485 A1. Claim 31 reads as follows:

> A method of treating a bone disease in a mammal comprising administering a therapeutically effective amount of a modulator of an osteoprotegerin binding protein.

Claims 32 and 33 depend from Claim 31 and recite a modulator as being a soluble form of an osteoprotegerin binding protein (hereafter "OPGbp") (Claim 32) or an antibody, or fragment thereof, which specifically binds an OPGbp.

The Examiner argues that, although Claim 31 of the '569 application recites "a method of treating a bone disease", it is not deemed patentably distinct from "a method of inhibiting bone resorption" in Claim 37 or "a method of inhibiting osteoclastogeneis" in Claim 52 of the present application.

Applicant points out that the above-referenced application has been allowed to go abandoned, as evidenced by the Notice of Abandonment dated December 29, 2004 and attached hereto as Exhibit A. The rejection may be withdrawn.

Rejection of Claims 37, 39-52 and 54-69 under 35 U.S.C. 112, first paragraph (enablement)

Claims 37, 39-52 and 54-69 are rejected under 35 U.S.C. 112, first paragraph, because the specification allegedly does not enable antagonist antibodies or fragments which bind OPGbp from residues 1-317 of SEQ ID NO:39. The Examiner argues that

making and isolating an antagonist antibody with therapeutic activity is highly unpredictable and therefore, in the absence of guidance from the specification, undue experimentation would be required to identify new OPGbp antibodies and screen them for therapeutic activity. The Examiner cites factors set forth in *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988) that may be considered in determining whether undue experimentation is required. Applicant disagrees.

The application provides sufficient guidance for making and isolating an OPGbp antagonist antibody with therapeutic activity. In the first instance, the specification teaches the structure of both the human and murine OPGbp and provides examples of potential forms of OPGbp that could be used to raise antibodies, including murine OPGbp from amino acid residues 158-316, a peptide from the BB'loop region of murine OPGbp, and a peptide from the EF loop region of murine OPGbp (see Example 10).

The Declaration of John K. Sullivan submitted on August 18, 2000 demonstrates that antibodies raised to human OPGbp (amino acid residues 159-317) and the human BB' loop and EF loop regions are able to inhibit osteoclastogenesis and bone resorption.

It is contemplated in the specification that other forms of OPGbp, including full length OPGbp (residues 1 to 317 for human OPGbp), may be used to raise antibodies (see p. 17, line 20 of the specification). As the specification taught that fragments of OPGbp could be used to raise antibodies, full length OPGbp may also be used to obtain OPGbp antibodies without undue experimentation. Moreover, full-length OPGbp contains within it the region of residues 159 to 317 as well as the BB' loop region and the EF loop region which were used to produce antagonist antibodies as described in the declaration of John K. Sullivan.

The specification also teaches assays which may be used to evaluate whether an OPGbp antibody inhibits bone resorption or inhibits osteoclastogenesis. Example 8 describes an *in vitro* assay for osteoclast formation which is suitable for detecting inhibition of osteoclastogenesis. Example 9 discloses an in vivo assay suitable for detecting inhibition of bone resorption. The use of such assays to test antibodies for

antagonist activity involves routine screening that is well within the capabilities of one skilled in the art and would not involve undue experimentation. As was stated in *Wands*:

> The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibodies with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas to find one that makes the desired antibody (*Wands* at 1406).

The disclosure of the OPGbp antigen and assays for measuring osteoclastogenesis and bone resorption allows one skilled in the art to identify additional OPGbp antibodies with desired characteristics without undue experimentation.

Rejection of Claims 37, 39-52 and 54-69 under 35 U.S.C. 112, first paragraph (written description)

Claims 37, 39-52 and 54-69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventor(s) had possession of the claimed invention. The Examiner argues that the independent claims (Claims 37 and 52) recite a genus of antibodies which bind to a target having residues 1 to 317 of SEQ ID NO:39. The Examiner further alleges that although the disclosure provides the target specificity for the claimed antibodies, such a disclosure by itself does not adequately describe the genus of antibodies.

The Examiner relies on the decision in *Noelle v. Lederman et al.* (69 USPQ2d 1508 (Fed. Cir. 2004) to support his position. In particular, the Examiner quotes the following:

> Therefore, based on our past precedent, as long as an applicant has disclosed a 'fully characterized antigen either by its structure, formula, chemical name or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.

Applicant maintains that the Examiner has misapplied the decision in *Noelle* to the present case. Noelle disclosed an antibody which bound to activated mouse T cells and, based on this disclosure, sought to claim an antibody which bound to any CD40CR polypeptide. Further, Noelle sought to claim an antibody which bound to human CD40CR. The Federal Circuit found that Noelle failed to describe human CD40CR because his application lacked any structural information, and therefore failed to describe the genus of antibodies which bind to human CD40CR. Likewise, Noelle failed to describe the genus of CD40CR polypeptides encompassed by his claims because he provided only a single example of a CD40CR polypeptide, namely murine CD40CR. According to the Federal Circuit, what was clearly lacking in Noelle's disclosure was a fully characterized target for an antibody.

By contrast, Applicant has claimed an antibody which binds to human OPGbp of SEQ ID NO:39. The specification fully characterizes the antigen by providing its full DNA and amino acid sequence and therefore satisfies the written description requirement for antibodies binding to said antigen, consistent with the decision in *Noelle*. The rejection may be withdrawn.

Rejection of Claims 43 and 58 under 35 U.S.C. 112, first paragraph (written description)

Claims 43 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventor(s) had possession of the claimed invention. The Examiner argues that the antibodies used in the claimed methods be "prepared by immunization of a transgenic animal capable of producing human antibodies" did not exist as of the time of filing of the instant specification and therefore must be made. The Examiner also argues that the claimed genus of antibodies is not sufficiently described as there is no disclosure in the specification of structure, physical or chemical characteristics, functional characteristics, and so forth, of the claimed antibodies.

Applicant notes that in fact transgenic mice capable of producing human antibodies were known as of the earliest filing date of the application. On p. 17, line 31

of the specification, reference is made to PCT Publication No. WO93/12227 which describes transgenic mice and methods for making such mice. Thus, it would not have been necessary to actually construct such mice.

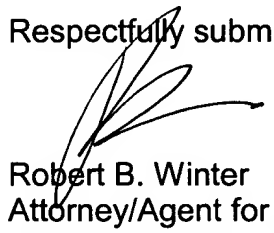
The antibodies of Claims 43 and 58 are claimed not only by the process by which they are made but also by binding to OPGbp of SEQ ID NO:39. As indicated above in the previous rejection under 35 U.S.C. 112, first paragraph (written description), antibodies which bind to OPGbp which is characterized by its amino acid sequence meet the written description requirement.

Applicant acknowledges the citation by the Examiner of U.S. 6,645,500 B1, which reference is not relied upon for the instant rejection(s) but is considered by the Examiner to be pertinent to the instant application.

CONCLUSION

Claims 37-69 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,



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